HYPERTROPHIC NODULAR GLIOSIS.

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Hypertrophic nodular gliosis of the brain does not appear to have escaped entirely the notice of the older writers, although their descriptions of, or, rather, their allusions to, this condition are so vague and unsatisfactory that it is impossible to be altogether sure of this fact. Bourneville was the first to give a clear description of the disease, and his earliest case was published as recently as 1880. A number of cases have since been published, but only a few have been carefully studied, and it appeared desirable, therefore, to place the following example upon record:

J. H., white, male, was admitted to the Pennsylvania Traning School for Feeble-Minded Children, on November 2d, 1888. An imperfect history was obtained from a member of the Board of the Children's Aid Society. The boy's father was born in Massachusetts; he was a plumber, and addicted to the use of alcohol. His mother was born in Ireland, and seems to have had no neuropathic condition; it is stated that she died of cancer of the breast at the age of 50. Nothing is known of the grandparents. The patient was the last of four children; two brothers are dead; cause, unknown; one sister was placed in a hospital for the insane at the age of thirteen. The patient was born at full term after a normal labor. He

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NOTE.—I desire to express my thanks to Dr. Martin W. Barr and to Dr. Frank White of the Pennsylvania Training School for Feeble-Minded Children, who have kindly placed the clinical history of this case at my disposal. The microscopical work has all been done at the Pepper Clinical Laboratory.

was apparently healthy until ten months old, when he began to have occasional spasms, which occurred more frequently as he grew older. He did not walk until four years of age. His gait was always rather slow and unsteady, and the power of coördination poor. He was able to say two or three words, but those were spoken very indistinctly.

The following notes were made on September 10th, 1896:

"J. H., aged fifteen, low-grade idiot and epileptic, body fairly well nourished, muscular system poorly developed, cutaneous reflexes apparently normal, cremasteric reflexes increased, patellar reflexes exaggerated, tactile sensibility apparently normal, thermal sensibility uncertain. The eyes are myopic; the pupils react to light. Hearing is probably good. The head sphacecephalic but symmetrical; Romberg's symptom is present. Since admission he has been treated for epilepsy, purulent otorrhœa and prolapse of rectum." The following notes are given in regard to his general condition: "He is totally dependent in every way, being unable to feed himself. When food is placed in his mouth he makes little effort at mastication, so that it is necessary to give him liquid or soft diet. He sometimes drinks a large amount of water at one time, but it seems to run into the stomach from gravity, there being no effort on his part to swallow, and it does not seem to alleviate his thirst. He was subject to merycism. There was often considerable protrusion of the rectum. He was an onanist; the habit being apparently more pronounced before an epileptic attack. For some hours previous to the outbreak of a spasm he would bark like a dog. When taken with a fit, if standing, he would fall instantly, the right side of the head striking first. During the seizure the muscles of the right side of the face showed quick, spasmodic movements; the left side remained in tonic contraction; the right hand was open and the left clenched, and the muscles of the left forearm continued spastic for some time following the spasm. After the spasm he would laugh in a silly fashion an hour or more. Before the spasm he was irritable and restless, but apparently more intelligent than at other times. His last illness began in December. It commenced with an almost constant succession of spasms, 63 occurring in two hours. They were general, but, as a rule, more severe on the right side; the head was turned to the right; the left arm was rigid and lay in the bed; the right arm was rigid and elevated; the left leg twitched, the right was rigid; the hands were flexed at the wrist; the fingers fully extended. The spasms decreased to about 10 or 12 per hour, and in the course of 24 hours the patient died from exhaustion."

The *autopsy* was performed on the 10th of December, 1896, about 24 hours after death. The following notes were taken:

Body of boy moderately emaciated, no rigor mortis, no postmortem lividity. The testicles were still in the inguinal canal; there was a bruise on the forehead and a deep cut on the chin, penetrating almost to the bone. There were numerous petechiæ on the surface of the abdomen. The meninges of the spinal cord contained a considerable amount of fat; they were not injected, and there was no abnormal collection of cerebrospinal fluid. The substance of the cord was firm. The skull was slightly thickened; the dura mater was firmly adherent, but there were no signs of inflammation. The pia mater was smooth, transparent, and stripped easily. In the cortex of the cerebral hemispheres were a number of sharply circumscribed areas much denser than the normal brain tissue. These were pale, slightly protuberant, and the large ones slightly depressed in the centre. When incised, the surface of the section was seen to be grayish white, firm and dry. The nodules appeared to extend a short distance into the white matter, but the distinction between the medulla and the cortex was preserved. The ventricles were not dilated, but upon the floor of the lateral ventricles were a number of small, white nodules, a few mm.

in diameter, projecting distinctly above the surface. The circle of Willis was normal. There was a hemorrhage into the floor of the fourth ventricle. The whole brain appeared to be larger than normal. The abdominal organs were normal in arrangement. There were some pleural adhesions and moderate hypostatic congestion in both lungs. The heart was small; the left ventricle moderately hypertrophied, and there was slight sclerosis at the bases of the aortic valves; the mitral valve admitted one finger; the aorta was elastic and smooth. The heart contained numerous chicken fat clots. The surface of the duodenum was covered by numerous small nodules of varying size, quite firm in consistency. The rest of the intestinal tract showed no gross morbid changes. The mesenteric glands were greatly enlarged. Both adrenal capsules showed advanced fatty degeneration of the cortex. The right kidney contained a huge tumor-like mass about 7 cm. in diameter, that seemed to replace a portion of its substance, and numerous small nodules. The surface of the tumor was smooth and white, and did not exude any juice; the growth was sharply circumscribed; its consistency was exceedingly dense. The small nodules were similar in character. The capsule of the kidney was adherent; the cortex was pale, narrowed, granular, and contained numerous cysts, and the renal vessels were injected. The left kidney contained small nodules, in all respects similar to those of the right, and the kidney substance showed the same changes. The liver was greatly enlarged. The left lobe extended to the left posterior axillary line, overlying the spleen; upon the surface there were numerous whitish discolorations. Upon section, it appeared to be normal. The mucous membrane of the stomach was thickened, rugous and somewhat pale. The mucous membrane of the duodenum contained a number of small, hard nodules. The rest of the intestinal tract was normal. The pancreas was soft, and showed no changes. The bladder contained turbid urine, probably due to precipitation of the urates, for the mucous membrane was smooth. The thyroid gland was apparently normal. The thymus gland was present. The thoracic and cervical lymph glands were enlarged. The tumors of the kidney were composed of spindle cells, some with round or oval nuclei, and others with rod-shaped nuclei that resembled non-striated muscular fibres.

Microscopically, it was seen that the growths infiltrated the surrounding tissues, and a number of the renal tubules in the neighborhood exhibited proliferation of the epithelial cells. The tumors were therefore diagnosed adenosarcomata of the kidney, although neither cartilage nor striated muscular tissue was found. According to Birch-Hirschfeld, these tumors commence in fetal life, and may attain considerable size in childhood, and ultimately, if death does not occur too early, give rise to metastasis. Sections through the wall of the duodenum showed that the various layers were normal, with the exception of the mucosa. In this the tumors were represented by masses staining a diffuse blue with hæmatoxylin; the central part was pale; the peripheral darker. There was no distinct structure to be found in these masses, but, as they faded into the surrounding tissue, small, round cells became more distinct. The condition represents hyperplasia of the lymph follicles, possibly sarcomatous in nature, which accounts for the distinct involvement of the capsule, although the extreme degeneration of the tissue renders it impossible to speak positively. There was no evidence of metastasis in any other part of the body. A more minute examination of the brain after hardening in Müller's fluid showed the following changes: The pia stripped readily; the nodules were slightly elevated, hard, paler than the surrounding tissue, and the surface exhibited slight granulation. The membranes were not thickened nor congested. When incised, the dense tissue involved all of the cortex, which was usually increased in thickness, and extended a few millimeters into the white substance.

The distinction between cortex and medulla was maintained, chiefly by the greater retractibility of the latter. There was no appearance of congestion in the morbid tissue. The areas of gliosis are very irregular in shape and very unequal in size, ranging from 0.5 cm. to 7 cm. in diameter. They are distributed as follows:

Left Cerebral Hemisphere.—Convex surface in the superior frontal convolution; at the anterior end a small nodule; in the middle a group of three small nodules; at the posterior end a large nodule that extends to the median surface. In the second frontal convolution, at the anterior end, a large sclerotic patch involving four small convolutions; just back of these is a smaller mass, and at the posterior end a large mass that extends along a small annectant gyrus, and involves the ascending frontal gyrus. In the third frontal convolution the operculum is normal; the anterior part is occupied by a huge sclerotic mass, 5x7 cm. in extent, involving a number of secondary gyri. In the ascending frontal convolution there is only the nodule that extends from the second frontal. In the ascending parietal there is a small nodule about the centre, near the fissure of Rolando, and a larger one near the longitudinal fissure, and a still larger one in the posterior portion of the superior parietal, about 3x6 cm. in area. The supramarginal gyrus contains a small mass in the anterior limb, and the whole of the angular gyrus appears to be converted into a single sclerotic mass, perhaps the largest in the brain. The occipital lobe is composed of a number of nodules of various sizes, separated by small areas of softer tissue, none of the convolutions being entirely normal. In the first tempero-sphenoidal convolution there is a small nodule in the posterior end; the second is completely sclerosed anteriorly; in the third there is a small nodular mass at the anterior, and two at the posterior extremity; in the fourth there is a mass of gliosis, posteriorly extending into the occipital lobe. The fifth convolution is apparently normal.

The Internal Surface.—There are large nodules in the anterior and posterior part of the first frontal convolution, numerous nodules in the quadrate lobule; a large mass in the posterior portion of the cuneus, and a few nodules on the orbital surface of the frontal lobe. The cornu ammonis is apparently normal.

Right Cerebral Hemisphere.—In the superior frontal convolution there are several nodules in the anterior portion, a large mass in the middle, and another posteriorly. In the third frontal convolution there is a mass in the anterior portion. The operculum is not involved. There is a nodule in the lower extremity of the ascending frontal convolution. In the superior parietal there are a few nodules posteriorly. The supramarginal gyrus is involved throughout. The occipital lobe resembles that of the left side. The anterior portions of the first, second and fourth tempero-sphenoidal convolutions contain some nodules. The cornu ammonis is normal. On the internal surface there is a mass of gliosis in the posterior part of the cuneus. The calloso-marginal convolution contains a few scattered nodules. There is a large mass in the posterior part and another in the middle of the superior frontal convolution, and a few small nodules in the orbital extension of the second frontal. The cerebellum, pons and medulla are apparently uninvolved. In the interior of the brain, areas of sclerosis large enough to be detected with the naked eye cannot be found, excepting the nodules already described upon the surfaces of the ventricles. The third and fourth ventricles are free, and the basal ganglia, as far as examined by horizontal section through the brain, are not affected. The pyramids and olives in the medulla are quite distinct. The peduncles and corpora mammillaria are of equal size. The cerebellum is of normal size and consistency. There are no gross lesions of the cord.

The microscopical appearances were as follows: When the sclerotic areas were stained with hæmatoxylin and eosin the following changes were observed: The neuroglia was composed of coarse fibres, forming a coarse-meshed reticulum, or else arranged in bands, or twisted into a sort of spiral form; these changes were particularly noticeable either just beneath the pia mater, or about the junction of the gray and white matter; the neuroglia cells were somewhat smaller than normal, irregular in outline, and moderately increased in number. In those situations where the sclerosis was greater, the vessels were greatly increased in number; beneath the pia, however, the sclerotic areas seemed to be less vascular than normal. Nearly all these blood vessels were distended with blood, a result, I suppose, of the violent muscular effort occuring during the status epilepticus. They appeared to be much larger than normal, and the walls often showed proliferation of the nuclei. The perivascular spaces were frequently distended, sometimes exceeding in width the diameter of the vessels. Occasionally they were filled with a delicate reticulum, although it could not be determined that this was composed of neuroglia fibres. There was no accumulation of round cells in the perivascular spaces, but occasionally large cells could be seen that contained granules staining black with osmic acid. These are probably connective tissue cells that have absorbed fatty detritus, perhaps resulting from a degeneration of the myelin sheaths. When the vessels were cut longitudinally, it could be seen that they were moderately tortuous, but they did not show any aneurismal dilations. In sections stained by Rosin's method they appeared quite red, partly due to the staining of the red blood vessels; but in the more sclerotic areas the walls also appeared to have taken this color, and it may be that they have undergone hyalin degeneration, particularly as the sections stained by Van Gieson's method showed the same peculiarities. Amylaceous bodies were not observed in the cortical lesions. The nerve cells stained fairly well; they were present in all the areas of sclerosis, excepting those few where the bundles of neuroglia were arranged in wavy bands or spirals and permeated by large and numerous vessels. Neither by carmine nor hæmatoxylin did they show any signs of degeneration, but they appeared to be more irregularly placed than usual. This alteration was still more pronounced in the sections that had been stained by Nissl's method, in which it could be seen that the apices of the pyramidal cells pointed in all directions. They were very numerous, even more so, apparently, than normal, and stained rather deeply; their processes were slightly tortuous, but there were no definite nuclear changes and no alterations in the protoplasm. In position they seemed to be abnormal, large cells being found in the second layer as well as the third. A number of sections were also stained by Berkeley's modification of Golgi's method. The neuroglia cells appeared to be very numerous, and impregnated very distinctly. The pyramidal cells were only found in a few sections, in which they seemed to be perfectly normal. The method is, however, so unsatisfactory for pathological purposes, that its only value in the present instance is to show that normal cells exist in the sclerotic areas. In some parts of the cortex certain peculiar bodies were observed in considerable number, that were circular or pear-shaped and very pale, appearing like vacuoles in the midst of the neuroglia tissue. Each contained a small, faintly staining, round nucleus in the centre, and probably represented a degenerated cell; but whether they are derived from the ganglion or the neuroglia cells, it is quite impossible to say. A number of sections were stained by the Weigert or Pal methods. In nearly all these the tangential fibres of the cortex were absent. Toward the white matter the cortex remained perfectly pale, with the exception of a few delicate fibres that passed irregularly through it. When the gliosis invaded the white matter, it did not in general cause complete destruction of the myelin sheaths, but the distance between the individual fibres was considerable, and gave rise

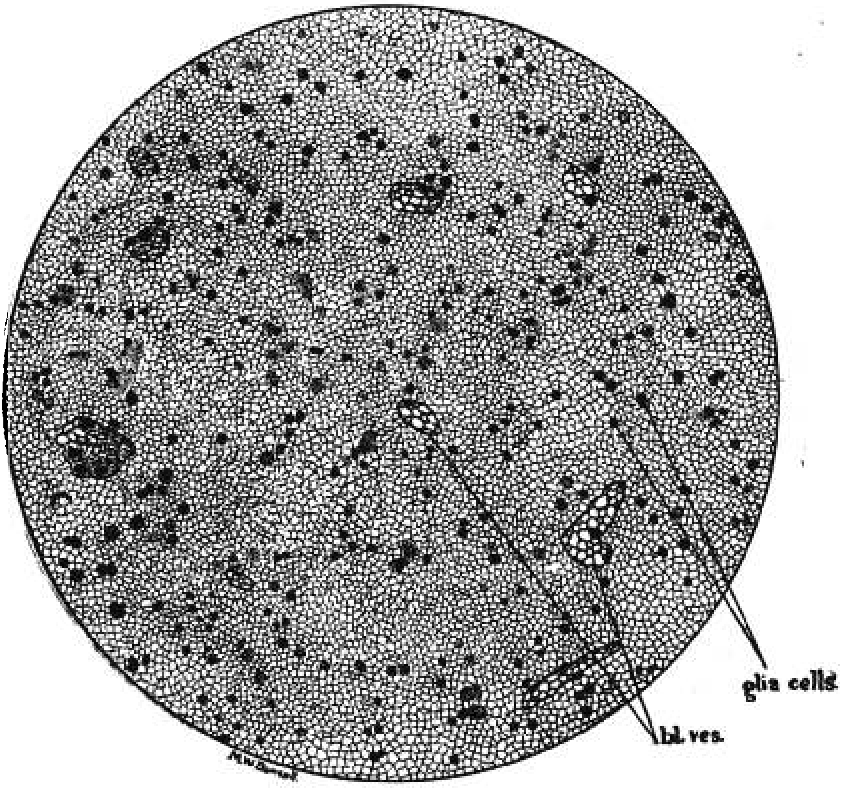

Fig. 1

Section through a sclerotic area in the third frontal convolution of the right side. The focus is about 4 mm. in diameter and situated at the junction of the cortex and white matter. It contains an excessive number of blood vessels, the neuroglia cells are more thickly placed than is normal, and the neuroglia fibres are coarser and form a looser meshwork. (Hæmatoxylin and eosin. Zeiss DD; oc. 3.)

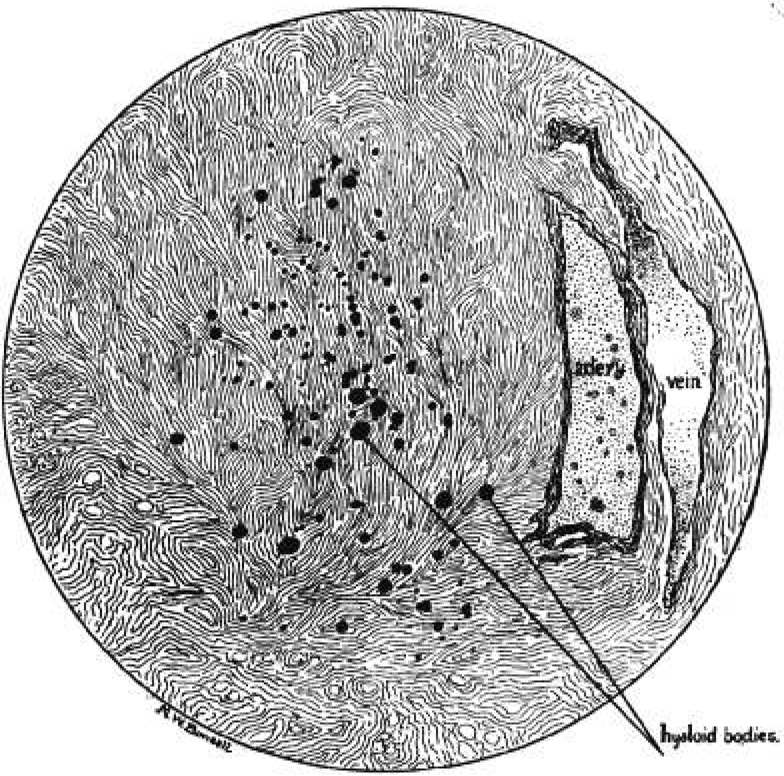

Fig. 2

Section through a nodule in the floor of the right lateral ventricle containing hyaloid bodies. Van Gieson's stain. (Zeiss AA; oc. 3.)

to an extremely feathery appearance at the junction of the white matter and the cortex. In these areas the sections appeared to be much paler than in other parts. The fibres of association could not be made out, and were probably largely lacking. Where the sclerosis was most advanced no myelinated fibres could be found. No degenerated fibres were found by Marchi's method, but a few cells containing black granules were observed in the perivascular spaces.

The nodules upon the floor of the lateral ventricles consisted of almost pure neuroglia tissue, arranged in bands, or in whorls twisted about the centre of the nodule. The blood vessels were greatly increased in number throughout the majority of these sclerotic areas, and in the sections stained by Van Gieson's method, exhibited the same changes as those in the cortex. In one of the nodules on the left side, there were a number of peculiar, irregular bodies, that were usually circular in shape, although sometimes slightly elongated, and showed a distinctly concentric structure. They stained deep blue with hæmatoxylin, remained a deep brown color in the sections stained by Weigert's method; they retained the stain by Gram's method, and with thionin and acid fuchsin stained bluish green with a delicate red border; they stained a deep red by Van Geison's method, and bright red with gentian violet. They were not soluble in alkaline or acid solutions. I am inclined to believe, on account of their situation beneath the ependyma and their peculiar staining reactions, that they represent agglomerations of altered amyloid material. They do not, however, stain brown with iodine. I have observed exactly similar bodies in an area of softening in the brain of a child that died of tubercular meningitis, and others somewhat similar in a case of paralysis agitans with marked arterial sclerosis. They appear, therefore, to indicate degeneration of nervous tissue, a view held by Stroebe and also by Dagonet, who regards them as a derivative of cerebrin. Beyond these nodules the hyperplastic neuroglia tissue extends deeply into the optic thalamus, showing the same thickening of the fibres and coarse meshing that was found in the sclerotic areas of the cortex. The ependyma covering the nodules was considerably wrinkled, giving, in cross section, a slightly papilomatous appearance; it was composed of a single layer of polygonal cells with deeply staining nuclei, that showed no evidences of proliferation, such as are present in neoplastic and inflammatory processes; the appearance bore a striking resemblance to that often seen in the intima of sclerotic arteries, and was probably due to retraction of the neuroglia tissue. In the cerebellum quantitative changes were distinctly seen. The cells of Purkinje were sometimes widely scattered, sometimes close together. They stained bright red with eosin; the nucleus showed a faint bluish tinge, was irregular in outline, and apparently contained very little chromatin. The medullated fibres were much fewer than ordinarily observed, and none at all were found in the cortical layer. The vessels in the cerebellum were not particularly numerous, and did not show the perivascular spaces. The pons was apparently normal. Along the edge of the left pyramidal tract in the medulla was a small area of sclerosis, sharply defined from the rest of the tract. The neuroglia cells appeared to be increased in number, and there was the same reticular arrangement of the neuroglia fibres. Otherwise the process resembled more closely a patch of insular sclerosis. In the spinal cord (lower cervical region) no distinct changes were noted, excepting on the left side, just outside the anterior cornua, where there were a number of dilated blood vessels, somewhat tortuous in their course, and a slight proliferation of the neuroglia tissue, staining red with acid fuchsin. Sections stained by the Weigert, Pal and Marchi methods, and by carmine, failed to show any trace of degeneration. The ganglion cells of the anterior cornua were normal. The central canal still existed as a microscopical channel.

An examination of the literature for similar cases has yielded the following results. It must not be understood, however, that all the cases of which I give abstracts were reported as tuberous gliosis. Some have been included under the title of hereditary syphilitic disease, and others have been described as cases of insular sclerosis.

The negative testimony is not uninteresting. Echeverria, whose book upon epilepsy appeared in 1870, and was the best monograph that had hitherto been published upon the subject in America, makes no mention of any lesion similar to this, although he describes quite extensively the pathological change found in epileptic brains:

Case I.—Bourneville. The patient was a female without neuropathic heredity. Convulsions commenced in infancy, and at the age of two years assumed the form of typical epilepsy. She never learned to walk nor talk, and when she was admitted to the hospital, at the age of fifteen years, it was found that the right arm and leg were flexed and partially atrophic. The epileptic attacks were Jacksonian in type, the spasm commencing in the right eye, which was drawn up and to the right; then rigidity of the right arm, followed by clonic spasm of the right arm and eyelids. At the autopsy the brain was large and slightly asymmetrical, the right peduncle and corpus mammillare being larger than the left. The pyramids were united with the olives; the pia mater was delicate and slightly adherent over the focal lesions. In the cortex of both cerebral hemispheres were numerous rounded masses of various sizes, white, opaque, firmer than the brain substance, and slightly prominent, with a shallow umbilication in the centre of the larger ones; the cornua ammonis were normal. The lungs were pneumonic; the left ventricle of the heart hypertrophied, and white nodular masses, apparently cancerous in structure, were found in both kidneys.

Case II.—Bourneville and Brissaud. The patient was a male; two other children were healthy. The mother had had convulsions during pregnancy. The child learned to walk at the age of two years, but could not speak. He had frequent epileptic attacks, during which he was cyanosed, and later this condition became permanent. There was a loud cardiac murmur. Death occurred at the age of four years, apparently from cardiac insufficiency. There was a large area of softening in the right frontal lobe, over which the pia mater was adherent. The sclerotic areas were found in both hemispheres, but were more numerous on the left side. There was a congenital lesion of the heart. Microscopic examination of the brain substance showed the absence of nervous elements in the sclerotic tissue. The glia cells were increased in number, but were somewhat irregular in shape. There was no sharp line of demarkation between the sclerotic and normal tissue, but the ganglion cells in the neighborhood of the lesions were granular and yellow; the blood vessels were few but large, and Brissaud, who made the examination, declares that medullated fibres were absent in the lesions, but he used only the carmine stain.

Case III.—Bourneville and Bonnaire. The patient was a male, the tenth of thirteen children, of whom only three others, all of whom appeared to be normal, lived for any considerable time after birth. There was neuropathic family history. The child was apparently normal for the first five months, and then received a severe injury to the head, which was followed by a notable change in its disposition. Convulsions, during which the child would become rigid for about 15 minutes, without loss of consciousness, commenced at the age of seven and a half months. He did not walk until two years and a half old, could not talk, recognize his parents nor feed himself. He died at the age of five years. The brain weighed 1,040 grms.; the dura mater was adherent to the calvarium. The pia mater was injected, but not adherent. The sclerotic nodules were found in the cortex and in the corpus striatum. Numerous round tumors were found in the kidney, which proved to be encephaloid sarcoma. There were no lesions in the isthmus or cerebellum, and the ventricles were not dilated.

Case IV.—Bourneville and Bonnaire. The patient was a male, the fourth of seven children, only three of whom lived beyond the age of infancy. There was marked neuropathic heredity, and both father and mother had had skin eruptions. The child was born at the sixth month, and had signs of scrofula. Convulsions were first noted in the sixth week, and recurred frequently. At the age of two years there was paresis of the neck and arms, but this disappeared two years later. The child never could walk without support, and there was a tendency to fall forward. It was an imbecile and filthy in its habits, the only manifestation of intelligence being the occasional expression of pleasure. Death occurred at the age of five years in status epilepticus. The sclerotic nodules were found in the cortex and basal ganglia. The occipital region of the brain was slightly flattened. The kidneys contained numerous serous cysts and raised tumors, that were soft and white.

Case V.—Bourneville and Bonnaire. The patient was a male, with neuropathic family history; two children were dead, two others lived, and were apparently healthy. There was no history of syphilis or injury. Convulsions commenced at the age of five years and nine months. The sclerotic nodules were found in the cortex of the hemispheres and in the caudate nuclei. The kidneys contained cysts and some large, firm tumors.

Case VI.—Hartdegen. The patient was a male, asphyxiated at birth and unable to nurse or to swallow. The anterior fontanelle was dilated, and there was a lumbosacral spina bifida that became infected, giving rise to a leptomeningitis, apparently the cause of death, which occurred at the age of forty-eight hours. Numerous sclerotic nodules were found on the surface of the hemispheres, which were firmer, paler and dryer than the brain substance. Smaller nodules were found in the walls of the ventricles. The thoracic and abdominal organs were normal. Microscopically, the sclerotic areas consisted of a finely granular tissue containing delicate fibres. The sclerotic lesions contained numerous ganglion cells that were irregular in shape and abnormal in position, some of the largest being found in the most superficial layer of the cortex. The nodules in the lateral ventricles consisted of large cells with numerous processes, that were mingled with fibres of connective tissue, extending downward from the ependyma. He regards these growths as *glioma ganglionare cerebri congenitum.* The ventricles were dilated. The convolutions were normal in arrangement.

Case VII.—Pollak. The patient was a female, whose mother had had severe headache and attacks of dizziness during pregnancy. Two other children were healthy; one had died of epileptic attacks. Convulsions occurred four days after birth, accompanied by fever and œdema of the scalp; this continued four days, after which the child seemed paretic, no spontaneous movements being observed excepting a slight twitching of the facial muscles when loud noises were made. Deglutition was always difficult, and the patient showed a marked aversion to liquids, especially water, never drinking, although she had constant polyuria. In spite of this, she was well nourished. As she grew older, she manifested pleasure when shown bright objects or when she heard music, and recognized her father's voice. There were occasional attacks of trembling, and paradoxical contraction was observed in the tibialis anticus and quadricep extensor. There was nystagmus, divergent strabismus and unequal pupils; the fixing eye was in extreme myosis and the other mydriatic. During the second dentition muscular atrophy commenced in the feet and hands. In the fourth year of her age chronic cramps occurred in the limbs; there were gnashing of the teeth and the signs of hydrocephalus, followed by death in a few months. At the autopsy it was found that the dura mater was adherent, the pia mater thickened and partially adherent. Pale, hard elevations were observed in the cerebral hemispheres, anterior to the ascending parietal convolution, and over these the pia mater was firmly adherent. The corpus callosum was thickened and nodular. The ventricles were rough, and the basal ganglia and spinal cord contained areas of sclerosis. No microscopical examination was made. Pollak calls the case one of congenital disseminated sclerosis, and claims that he made an ante-mortem diagnosis, although he appears to be unfamiliar with the nature of the process. Two years previously he reported a living case with similar, but less severe, symptoms.

Case VIII.—Bruckner. There was no neuropathic heredity, no history of injury or of syphilis. The patient was a girl, who commenced to speak in her second year and to walk in her fourth. At school she learned to write with great difficulty, and was always shy and timorous. She was never able to calculate. The first epileptic attack occurred in her ninth year. After this fits recurred occasionally, and there was some disturbance of the gait, which later improved. At the age of eighteen years, the patient became maniacal, and then passed rapidly into a state of apathetic idiocy, although sensation, motion and the vegetative organs remained normal. A year later epileptic attacks recommenced, but were quite infrequent. At the age of twenty-two years the patient died of phthisis. At the autopsy the brain was found to be large and to contain numerous circumscribed foci of hardening, the larger ones having depressed centres. They involved principally the gray matter, but also extended into the white substance. Microscopically, a coarse fibrous connective tissue was found, especially just beneath the pia mater, where it assumed the form of a band of wavy fibres. In places ganglion cells were observed, included in a fine-meshed reticulum, that were apparently normal, but more thickly placed than usual. The blood vessels were characterized by wide perivascular lymph spaces. The ventricles of the brain were distended, and from the ependyma a fine fibrous stroma extended inward, containing holes filled with large, glassy, round cells, between which were some chalky deposits.

Case IX.—Pozzi reports the case of a man admitted to the hospital, at the age of sixty-eight years, suffering from dementia, with occasional outbursts of maniacal violence, alternating with states of melancholic depression. There was a history of epilepsy, but nothing further could be ascertained about the patient. Shortly after admission, and two months before death, the epileptic attacks recurred with great frequency, and death was apparently due to "status epilepticus." At the autopsy the skull was thick, the dura mater partially adherent, the pia mater injected, but not adherent, and there was some subarachnoid effusion. In certain regions the convolutions were small, hard and granular; in others they were enlarged, hard and smooth, the enlargement being nodular in character. Brissaud examined the specimens microscopically, and reported that the hypertrophic areas resembled cirrhosis,the neuroglia forming a dense, non-vascular mass, harder than the brain tissue. The ganglion cells were not degenerated, but rarer than usual. The large motor cells could not be found. There was no disturbance of the normal succession of the layers of the cortex. The atrophic convolutions were similar in character, excepting that the neuroglia seemed to be denser and the ganglion cells even fewer. He also found certain round masses in the midst of the neuroglia, that he regarded as colloid in nature.

Case X.—Simon. The patient was a female, with neuropathic family history. At the age of two and one-half years she was admitted to the hospital, and it was noted that she was microcephalic and showed contractions of all four limbs. There was continual agitation of the muscles of the face and limbs and frequent attacks of epilepsy. The intelligence was almost nothing. The digestive functions, excepting deglutition, were normal. Death occurred one month after admission. At the autopsy two sclerotic nodules were found in each hemisphere, just in front of the fissure of Rolando. The convolutions in the neighborhood were atrophic. The sclerotic tissue extended two or three millimeters into the substance of the brain, and the microscopical examination showed proliferation of fibrous tissue, the destruction of the cells and of the myelin sheaths. There were secondary alterations in the pyramidal columns of the cord.

Case XI.—Schule. The sex of the patient is not given, and there is no family history. The epileptic attacks commenced at the age of three years. The patient was not a total idiot, and learned something at school. There was right-sided facial atrophy, the gait was normal, Romberg's sign was present, the speech was slow, and the hearing of the left ear imperfect. Death occurred in status epilepticus, at the age of sixteen years. The brain weighed 1,390 grams. The dura was adherent to the skull and the pia mater over the projecting sclerotic mass in the frontal region. The brain otherwise exhibited typical nodular sclerosis.

Case XII.—Buchholz describes the specimen from a case. The brain contained some nodules upon the surface of the convolutions and some cysts in the brain substance. There was round-cell infiltration around the vessels, as if the processes were inflammatory in nature. Some of the nodules were composed of true connective tissue, with spindle-shaped nuclei, and a similar tissue was found in the cysts. It is stated that some of the fibrous bands represented degenerated vessels.

Case XIII.—Thibal reported another case from the service of Bourneville, but I have been unable to obtain the original paper.

Cases XIV., XV., XVI.—Buchholz reports three doubtful cases. Two of the patients were epileptic males; in the brains of both of whom increase of the neuroglia cells and hyperplasia of the neuroglia tissues were found, and also degeneration of the ganglion cells. The changes were principally found in the cortex, but sometimes affected the white substance, and occasionally led to cavity formation, in which case compound granular cells were usually present. One of the brains weighed 1,575 grams. The third patient was a paranoiac woman, who had been married; her brain presented similar changes.

Cases XVII. to XXII.—Wilmarth. Six cases are mentioned as having been found in the brains of epileptics and idiots at the Training School for Feeble-Minded Children. In some, the situation of the sclerotic nodules in the motor region explained the symptoms. The descriptions are very meagre and unsatisfactory.

Case XXIII.—Henoch. The patient was included in a series of doubtful cases of cerebral syphilis. The child was admitted to the hospital at the age of two years, and presented a peculiar alternation of slyness and stupidity. There was spina ventosa, but no disturbance of motility. Death occurred from diphtheria. At the autopsy a number of rough tumors, about the size of cherries, were found in the substance of the brain and cerebellum. A similar growth was also found in the upper portion of the left kidney. There was some periostitis upon the surface of the tibia, and the tumors were declared by a pathologist to be gummata.

Case XXIV.—Berdez. The patient was a male, without neuropathic family history. Other children in the family were perfectly healthy. At the age of four months convulsive attacks occurred, in which the child became slightly rigid, and there were movements of the eyes, followed by periods of loss of consciousness. Later, these became more typically epileptic. The child never talked nor gave any signs of intelligence, and could not walk.

At the age of two years, when admitted to the hospital, the head was found to measure fifty-two centimeters in circumference. The pupils were normal; there were no muscular atrophies nor choreic movements of the extremities. A diagnosis of hydrocephalus was made, and craniotomy performed, which resulted in death. The brain was large, and presented the typical appearance of tuberous sclerosis, the nodules being found in both hemispheres, and one in each of the caudate nuclei. The ventricles were not distended, and their surface was smooth. The central canal of the cord was dilated. In the sclerotic areas the nerve cells and fibres were absent. In the neighborhood of the lesion they still existed, but appeared normal. Many of the cells were surrounded by large pericellular spaces. The lymphatic spaces were also distended, and the vessels were fewer than normal. The neuroglia appeared hyperplastic.

Case XXV.—Bourneville. The antecedents of the patient were distinctly neuropathic. Both the father and mother had had syphilis, and the latter had had numerous miscarriages. The first signs of mental deficiency were observed at the age of three months. At the age of thirty-three months a few words were spoken, and the patient made an effort to walk. Epileptic attacks commenced at the age of eight months, but soon ceased, and did not recur until the child was three years old. Death occurred at the age of eleven years. The pia mater was adherent to the cortex over the sclerotic nodules. These consisted of dense masses of neuroglia tissue, without nervous elements, although the neuroglia cells sometimes presented peculiar elongations, and contained fewer blood vessels than the normal tissue.

Case XXVI.—Tedeschi. The patient, a woman, lived to the age of twenty-eight years, and was married. She suffered from chronic epilepsy, and died from tuberculosis. The brain presented the characteristics of the disease. It was enlarged and firm, and about twenty nodules were distributed upon the surface of the hemispheres. Upon section of the sclerotic nodules, they were found to consist of a gray peripheral zone, a pale, white, median zone, and an intensely red centre. Beneath the ependyma were a number of hard swellings, about the size of millet seeds. The sclerotic areas contained a few faintly staining varicose fibres. The neuroglia cells possessed threadlike processes, and formed a thick network, and some of them resembled ganglion cells, having large, pale nuclei and some branching processes. There was hyperplasia of the blood vessels, but no round-celled infiltration. The masses in the floor of the ventricles were composed of cells with long, delicate processes, that formed a network permeated by normal vessels. The ganglion cells of the thickened gyri were vacuolated, and sometimes the nucleus was deformed and near the periphery. In the other areas large cells, fifty-four microns in diameter, with large, pale nuclei, degenerated protoplasm, and branching processes were found, which Tedeschi holds to be ganglion cells similar to those found in glioma.

Case XXVII.—Spiller. There was no family history. The patient was an imbecile, and was epileptic; during his fits he would fall, striking the right parietal region of the head. The history is extremely meagre. The age is not given. At the autopsy it was noted that both feet were in the equino-varus position. There were no contractures and only slight evidences of rachitis. The dura was not adherent. The brain was slightly œdematous, and contained a sclerotic area, about the size of a dollar, in the right frontal lobe. The cortex was narrowed. A similar area was found in the right parietal lobe. The other organs were normal.

Case XXVIII.—Jürgens. The family history was negative. Three weeks before delivery the mother had a slight fall. At the age of three months the child had a convulsion. This was repeated two weeks later. The child appeared, however, to have normal intelligence. Six weeks later general convulsions recommenced, and continued, with brief intervals, for several days. There was then paralysis of the right arm. The convulsions were repeated weekly, and were often associated with movements of the eyes, and preceded by a cry. The head was large, 41 cm., in circumference; the fontanelles were prominent and fluctuating. There was no disturbance of the reflexes and no contractures. Death occurred at the age of six months. At the autopsy the skull showed rachitic thickening; the dura mater was distended, but otherwise normal; the arachnoid and pia were thin and transparent; the convolutions were flattened, and many contained round, sharply circumscribed areas of a grayish white color and almost cartilaginous consistency. The upper surface of the lateral ventricles was rough, exhibiting here and there slight elevations, some almost as large as a cherry. The ependyma was thickened; sclerotic masses were also found in the basal ganglia. The spinal cord was normal, excepting the lower part of the lumbar region, which was slightly hardened. At the apex of the left ventricle there was a hard, spindle-form intumescence. Similar but smaller foci were scattered throughout the substance of the left ventricle, usually just beneath the pericardium. The mesenteric glands were enlarged; the kidneys contained cysts. Microscopical examination of the myocardial lesions showed sclerotic muscular fibres and areolar fibrous connective tissue, in the meshes of which were small, round or oval cysts resembling coccidia. Similar bodies were also found in the sclerotic areas in the brain. An emulsion of brain substance injected into three rabbits caused the death of two in two days without lesions, and of the third in eight days with typical parasitic myocarditis. Three rabbits were also inoculated in the eye, and one, at the time the paper was written, exhibited cerebrospinal symptoms.

Of these cases, the four reported by Buchholz and that of Henoch, should possibly be excluded as of some other nature.

In addition to these cases, similar pathological conditions are more or less definitely alluded to by other writers. Rokitansky speaks of the partial indurations of the brain, which are generally distinguished for the great degrees of hardness which they attain, and known as a callous state or cicatrix of the brain. These infiltrations, which he appears to regard as cancerous, sometimes render the diseased portion of the brain tough and firm, as if it were composed of fibrous tissue. According to Bourneville, Hayem, Hoffmann and D'Espine have referred to cases that may also be similar. Barlow and Bury also speak as if they had seen a number of examples, but give no details.

The common features of all these cases are, clinically, the existence of epilepsy with a greater or less impairment of the intelligence, and, pathologically, of a hyperplasia of the neuroglia, with the formation of tumorlike masses, and some destruction of the ganglion cells and nerve fibres. Hyperplasia of the neuroglia, without the formation of nodules, has also been described in epilepsy.

Chaslin examined three brains from epileptics, and found thickening and diffuse sclerosis of the cortex, that was due to a hyperplasia of the neurogliar cells and an increase of their fibres, which, he believes, may traverse the protoplasm of the cells, or be independent of them. The neuroglia seemed to invade, and, to a certain extent. to replace the surrounding structures, the most superficial layer of the cortex being chiefly affected. Often the nuclei of the neurogliar cells stained poorly, and their protoplasm showed a slight projection in one part. The ganglion cells were rare and irregularly arranged, and their protoplasmic processes altered. The vessels were usually normal, excepting in the sclerotic parts, where they were reduced in number and had thickened walls. The degree to which the process was advanced varied in different regions. Bleuler examined twenty-six brains obtained from chronic epileptics and idiots, in all of which the neuroglia was increased between the tangential fibres of the cortex and the pia mater. This change was diffuse, but not uniform, in all parts of the brain, and its extent appeared to correspond more closely to the degree of idiocy than to the duration of the disease. The pia was not adherent. In fifty-four brains taken from patients not epileptic, there were slight indications of the sclerosis in fifteen (idiots, paranoiacs, paralytics and senile dements), but even in these cases the appearance was not the same; the fibres were not parallel and were more loosely arranged. Schultze found hyperplasia of the neuroglia in a case of porencephaly, probably congenital in nature. Corpora amylacea and compound granular cells were also found in the lesions, and there were warty prominences upon the floors of the ventricles. Pierrot has observed sclerosis in senile brains, affecting the deepest and most superficial layers of the cortex.

Various theories have been held regarding the nature of gliosis. Brissaud, in discussing the case which he reported with Bourneville, speaks of it as a chronic inflammatory process of slow development, with its chief seat in the gray matter. 'In the following year, in discussing the case of Pozzi, he stated that the only distinction between the hypertrophic and atrophic forms is that the former represents an earlier stage, and the latter a later stage of the process; that is, hypertrophic sclerosis represents hyperplasia of the neuroglia cells and fibres, atrophic sclerosis their subsequent contraction.

Hartdegen, however, whose patient died two days after birth, pointed out that the process must be congenital; but, as in his case there was no defect in the arrangement of the convolutions, he held that it must have commenced after the seventh month of fœtal life, before which time the convolutions are not fully formed. Pollak is satisfied to call it disseminated sclerosis, which he believes may affect the fœtus in utero, developing slowly or rapidly after birth. Fürstner and Stühlinger had a theory of their own that to-day sounds somewhat absurd. They believed that the lymphocytes passed through the blood vessels and collected outside the adventitia, where they were converted into neuroglia cells, and that their gradual accumulation produced the sclerotic change. After this, pressure, or other cause, may produce softening in the centre of these areas; a process, they remark, and not unjustly, very similar to that which occurs in syringomyelia. They even claim to have observed these lymphocytes in the process of transformation. It should be noted that their specimens, all of which were from adults, showed distinct signs of inflammatory reaction. Chaslin, in 1889, believed that the sclerosis that occurs in epilepsy is due to a hyperplasia of the neuroglia, and proposed to call it neuroglia sclerosis. He points out that the neuroglia forms bundles of coarse fibres; an observation that had already been made by Buchholz, who explained it by supposing that the neuroglia cells were converted into fibres. In a paper published two years later he stated that he did not believe that the gliosis cerebri is due to an old inflammatory lesion, especially as the hyperplasia takes place at some distance from the blood vessels, and is most intense in the superficial layer, and nevertheless the pia is not adherent. He suggests three hypotheses: I. Arrest of development of the nerve cells and fibres. 2. Only partial development of the nerve tissue. 3. Primary development of the neuroglia and atrophy of the nerve tissue by compression. He preferred the last, particularly as he regards the process as congenital, and as, in the regions where it was advanced, the capillaries are compressed. He concluded that: 1. The fibres in the cerebral cortex in sclerosis are developed from the neuroglia. 2. This process is found in epilepsy, is due to some congenital defect, and should be called gliosis. 3. In many conditions in which it occurs several causes are active.

Féré appears to include sclerose tubereuse among the chronic forms of encephalitis, although he admits that

Chaslin has demonstrated that it is due to proliferation of the neuroglia tissue and is peculiar to the nervous system.

Birch-Hirschfeld has suggested the possibility that the primary lesion is an atrophy of the nervous elements with consecutive proliferation of the neuroglia tissues. He is skeptical regarding the inflammatory nature of the process. Ziegler also rejects the inflammatory theory, and holds to that of congenital defect; although he states that the form known as ependymal sclerosis, that is, the thickening of the subependymal neuroglia and its projection into the ventricle, a condition commonly present in gliosis cerebri, is usually associated with degenerative or inflammatory conditions. Thibal alone seems to consider nodular gliosis as a distinct disease, believing that there is a rapid hyperplasia of the neuroglia tissues, which presses upon the nervous elements and causes atrophy. A totally different view is taken by the English authors Barlow and Bury. They do not speak of tuberous sclerosis at all, but describe, among the changes occurring in the brain as a result of hereditary syphilis, conditions which are identical with it. The most striking and important lesions are found in the cortex. The sclerosis occurs in small masses, or may involve entire convolutions, with or without increase of their bulk. Sometimes there is a certain amount of atrophy, some of the convolutions being narrow, of cartilaginous consistency, and brownish pink in color. The white substance may be involved also, but ordinarily the change is entirely cortical. Microscopically there is found extensive overgrowth of the neuroglia and disappearance of the nerve cells; occasionally the membranes are adherent, and arterial changes are frequent, although not constant. Gowers, who appears to have devoted very little attention to this particular condition, adopts this view without hesitation. Henoch, although not suggesting any other etiology, does not believe that the cases are demonstrably syphilitic, an opinion with which most pathologists will agree. Barlow and Bury do not describe any cases, fail to mention whether syphilitic antecedents usually are present, or if unquestionable syphilitic lesions are to be found in other parts of the body.

Examination of the recorded cases with reference to the etiology gives very unsatisfactory results. In the great majority it is not discussed. Of all the twenty-seven cases the sex is given in seventeen, six female and eleven males; the presence or absence of neuropathic heredity is mentioned in nine cases, and may be inferred in a tenth; it was present in six. Traumatism occurred in one case, and appeared to bear some etiological relation to the condition. Syphilis of the parents is mentioned in one case, and it may have existed in another. In a number of others it was apparently excluded on account of the existence of other healthy children in the family, both older and younger. It is interesting to note the condition of the kidneys. This has been recorded in only eight cases; in a number of the others they were certainly not examined, and in the rest no mention is made of either the presence or absence of changes. Of these eight cases, tumors of the kidneys, essentially similar in their gross appearance, were found in five, and the kidneys of a sixth case contained cysts. In one case congenital lesions of the heart were present. In a case of Von Recklinghausen, which may possibly belong to this condition, multiple myomata of the heart were found. The discovery of a coccidial parasite by Jürgens is of great interest; but, although it is apparently pathogenic for rabbits, it cannot be accepted as the cause of the brain lesions without further confirmation. Unfortunately, these cases appear to be so rare that this is not likely soon to be forthcoming. The congenital character of some of the cases and the entire absence of any bodies resembling coccidia from the lesions justify, for the present, a certain degree of conservative skepticism.

An examination of the lesions, with particular reference to the nature of the process, shows that the following features are more or less constant in all of the cases: The thickening of the neuroglia fibres and their arrangement either in wavy lines or in coarse mesh work. Freund describes it as a hyperplasia of the neuroglia, with increase of the cells, and atrophy and partial or total disappearance of the nervous elements. The neuroglia forms a coarse-meshed network, or bundles that may subsequently retract. This is found not only in the forms of sclerosis that appear to be idiopathic, but also as a change secondary to destructive injuries and infectious diseases, such as syphilis. Tedeschi and I have both found it as a result of experimental injury. Koppen has found it in a number of cases that were usually of syphilitic nature. In one the lesions were found in the occipital lobes, limited particularly to the cortex, and consisted of small areas somewhat lighter and denser than the ordinary tissue. These were of two kinds—those containing granular cells and fibrous connective tissue, and showing traces of nervous tissue, and those consisting of proliferated neuroglia, in which the glia cells were increased in number, and their fibres formed a wide-meshed network; in these areas there was an excessive number of blood vessels, and the ganglion cells and nerve fibres had disappeared. In a brain with microgyri, probably a case of atrophic sclerosis, the neuroglia in some situations was arranged in irregular fibrous masses, sometimes in wavy, sometimes in spiral form. There was no network, and neither glia cells nor nerve fibres could be found. In the subependymal tissue similar changes were present. Weygandt also observed a coarse reticulum in the neuroglia in the neighborhood of a gumma of the brain, and in some of the neighboring convolutions the cortex contained an excess of glia cells. I have observed similar changes in the cortex of a brain from a habitual criminal, which, excepting an apparent thinness of the gray matter, exhibited no gross lesions.

The pyramidal cells are usually entirely absent in the most sclerotic foci; in other situations they are present, often apparently increased in number, and staining well, but they are atypical in arrangement, and show tortuosity of their protoplasmic processes, as occurred in my own case and in those of Hartdegen and Bruckner. The same condition has been described by Koster as occurring in the brain of an idiot who died at the age of twenty-six, and whose brain presented no gross lesions; by Bourneville and Pilliet, in a case of diffuse sclerosis of the brain and cord, and by Chaslin in his three epileptic brains. The pericellular spaces are occasionally distended. This, according to De Quervain, is not an antemortem condition, even although round cells are sometimes found in this space. Koster, however, looks upon it as a morbid lesion, having sometimes found two ganglion cells in one dilated space. It is certainly an artefact in many cases, however, and I do not personally believe that much weight can be attached to it. More important is the dilation of the perivascular spaces. Jendrassik and Marie were the first to call special attention to this. In their case this space was sometimes five or six times as wide as the vessel it surrounded, and was entirely occupied by a large-meshed reticular tissue, with cells at the intersections of the fibres that were not unlike neurogliar cells. The fibres either ceased at the inner surface of the lymphatic sheath, or they extended into the adventitia. The medullated nerve fibres stopped at the edge of the space as if cut off, and the vessels were tortuous and apparently more numerous than normal, both changes probably due to the retraction of the tissue. Muhr has described similar changes in a case of hemiatrophy of the brain. This distension of the perivascular lymph spaces seems to confirm Strümpell's theory of lymphatic obstruction.

The degree of vascularity has been variously described. Bourneville and Pilliet, and Tedeschi have found the blood vessels to be numerous, while Chaslin and Bourneville and Brissaud have stated that they are few, or absent from the sclerotic areas. Buchholz regards some of the fibrous tissue in his case as representing degenerated blood vessels. In my case both conditions were present. Where the sclerosis was slight, the blood vessels did not seem to be increased in number. Where it was marked, particularly in those areas found in the deepest layers of the cortex, they were distinctly more numerous. In fact, it sometimes appeared as if an agiomatous alteration had taken place. In the subependymal nodules, on the other hand, where the changes were by far the most pronounced, the blood vessels were entirely absent. It seems easy to understand how these variations occur. The proliferated neuroglia tissue must exert more or less pressure upon the surrounding tissue. In certain areas this pressure causes obstruction, with secondary dilatation of the blood vessels, and, perhaps, the approximation of certain adjacent branches. That an actual vascular proliferation takes place it is impossible to deny, but there seems to be no good reason to believe that it does, unless we accept the theory of Birch-Hirschfeld that there is a primary atrophy of the true nervous elements and secondary proliferation of the other tissues to take their place; but this theory appears to be disproved by the frequently reported presence of pyramidal cells and nerve fibres in those areas where the sclerosis has not reached an extreme degree. The ultimate disappearance of the blood vessels is probably due to their total obliteration by pressure. Comparing two neighboring nodules I saw numerous vessels in one, while in the other, in which the neuroglia fibres were coarser and the process appeared to be more advanced, they were totally absent. Perhaps the peculiar bodies found in the sclerotic areas beneath the ependyma of the lateral ventricles are more significant of the destruction of nerve tissue. Pozzi describes them, and calls them colloid, and they are probably the same as the round, glassy bodies that Bruckner mentions. Dagonet has described what are evidently the same things, and calls them hyaloid. He believes that they are derived from cerebrin. Stroebe found them in the cords of rabbits, in which partial or total section had been made, and from their relation to the nerve fibres is convinced that they are the products of the degeneration of the myelin sheaths and the axis cylinders. They have been frequently described in degenerative processes, and I have observed them in an area of softening in the brain of an infant that died of tubercular meningitis, and in the sclerotic areas in the cortex of the brain of a criminal. The peculiar pale, pear-shaped bodies found in the cortex are more difficult to explain. Bourneville, Tedeschi and De Quervain have found similar bodies and considered them as degenerated cells, either neuroglia or ganglion, an opinion with which I agree. If we consider them to be neuroglia cells, they suffice to explain the disappearance of these from the areas where the gliosis is most pronounced. In all the positive cases endarteritis and perivascular round-cell infiltration appear to have been absent.

It does not appear from this analysis that there is any ground for the assumption of either an inflammatory or syphilitic etiology. Either process can produce hyperplasia of the neuroglia tissue, but the absence of the round cells and proliferation of the true connective tissue, and the infrequency of pial adhesions are sufficient to exclude the former. Syphilis produces such a variety of lesions that it is difficult to state positively that it could not cause nodular gliosis. Von Bechterew, however, holds that syphilis of the nervous system is a disease of specific nature, caused directly by luetic infection, and not a condition which may develop as a result of preëxisting syphilis. In the case of disseminated syphilitic sclerosis that he reports, the focal lesions appear to have been due to proliferation of the perivascular connective tissue, and not to hyperplasia of the neuroglia, and there was extensive endarteritis. The inclusion of pure gliosis among the syphilitic conditions by Barlow and Bury seems wholly without warrant. The clinical histories are also negative; the fact that the parents of one child were certainly syphilitic is offset by the fact that in several cases we can be reasonably certain that they were not. The case of Henoch, in all likelihood, does not belong to this group; for in none of the others do the nodules bear the slightest resemblance to gummata. We are then forced to fall back upon some theory of the idiopathic proliferation of the neuroglia. In this connection it is interesting to note the considerable number of congenital defects that have been reported as occurring in these cases. In eight cases in which complete autopsies were made, tumors or cysts of the kidneys of considerable size were found in six. Unfortunately, satisfactory diagnoses have not been made in any of these cases with the exception of my own, although Bourneville speaks of one of his specimens as being cancerous, and Henoch of the nodules in his case as gummata. As the microscopic description of two of them at least agrees closely with the condition I observed, I think it not unlikely they were tumors similar to mine, that is, adenosarcomata of a distinctly congenital type. In no case except my own, as far as I am aware, were nodules found in any other part of the body. It seems to me therefore reasonable to conclude that hypertrophic tuberous gliosis is akin to tumor formation, and represents a growth peculiar to late fœtal existence in view of observations of Binswager and Hartdegen. It is closely allied to atrophic sclerosis, a condition most carefully described by Jendrassik and Marie, and to sclerosis with cavity formation. These varieties are not sharply separated, but any two, or all three, may coexist in the same brain. Bourneville has reported one case and Fürstner and Stühlinger two, in which cavities were found in sclerotic nodules, and in nearly all cases of the hypertrophic form some of the convolutions were atrophic.

The symptoms of this disease are exceedingly various. The essential ones are epilepsy, commencing in some form or other in early infancy, associated with a greater or less degree of idiocy. Richardière holds that in the hypertrophic form the convulsions are more frequent and severe, and the idiocy more profound, than in the atrophic form, but this is doubtful. It is said of Schule's case that she learned to read and write, although she was always unable to reckon; and Bruckner's patient learned to write a little. Tedeschi's subject was a married woman of 28. Pozzi's, an old man of 63, who had been able to keep out of an asylum for that many years. My own case exhibited remarkable skill in untying knots, no matter how complicated. The epilepsy also may be reduced to transient attacks of rigidity, as in Pollak's patient, or completely absent for long periods, as in Bruckner's case. The epileptic attacks, as far as one can gather from the often meagre reports, are sometimes Jacksonian in type, sometimes more general. The other symptoms, such as nystagmus, muscular atrophies, facial atrophy, are too infrequent to be seriously considered in making a diagnosis; difficulty of deglutition has been noted in Simon's and Pollak's cases, and in my own. The value of symptoms indicating focal lesions is doubtful. When the very considerable microscopic alteration of the cortex and the fact that the lesions are often found in the motor and visual regions are considered, it must be admitted that corresponding functional disturbances cannot exist. This is not improbable, in view of the frequent presence of the ganglion cells in the sclerotic areas of the cortex. Bourneville holds the clinical diagnosis to be exceedingly difficult. Freund, that it is impossible, claiming that the disease cannot be differentiated from diffuse atrophic sclerosis, or meningo-encephalitis; but Simon confidently describes the clinical course, and reports a number of living cases, as does also Richardière, although the latter admits the uncertainty of his diagnoses. Bruckner, in his own case, ascribes the idiocy to the involvement of the frontal lobes, and the epilepsy to the lesions in the motor region; but Simon's patient had no lesions in the frontal lobes, and was nevertheless an idiot, although it must be admitted that a certain degree of microcephaly might account for this. It is not unlikely, however, that the process, even in the hypertrophic nodular variety, is tolerably diffuse; for I have observed slight changes in portions of the cortex that are apparently normal. In my own case, the greater extent of the process on the left side may have been associated with the invariable tendency to fall to the right. Unfortunately, no accurate record of the condition of the eyes was kept, otherwise it is not impossible that the symmetrical lesions in the cuneus might have been suspected.

The following conclusions seem to be warranted:

I. There is a morbid process characterized by a hyperplasia of the neuroglia cells and fibres that leads to gradual atrophy of the nerve fibres and the ganglion cells, and is associated with perivascular changes of doubtful nature.

2. The first manifestations occur in early life, often a few weeks after birth, and anomalies or congenital tumors are sometimes found in the same cases.

3. All cases of this disease are epileptics, and many of them idiots.

4. The cause is unknown, but the disease probably commences before birth and after the seventh month of fœtal existence, and is of the same nature as gliomatosis.

Scarpatetti (Archiv für Psychiatrie, vol. 30, No. 2, p. 537) has recently reported an additional case of this nature. The father of the patient was unknown; the mother had always been sickly. The child had visited school in her youth and had learned something. In later life she had been at service, and had had three illegitimate children. The first is still living, the second died of hydrocephalus, the third she strangled. The investigation instituted by the court developed that she had suffered for years with occasional attacks of epilepsy. She was small, undeveloped and stupid. Her head had a circumference of 58 cm. There was a dermoid cyst on the left side of the nose; the ears were especially small, and there was torus palatinus. The patient was industrious, but appeared to take no interest in anything but her manual work. At the age of 20 she was attacked with fever, diarrhœa, pains in the legs, and paraplegia, dying on the third day of the attack. At the autopsy the skull was found to be thick and solid, the dura slightly adherent. In the substance of the brain were four hard, tumorlike masses, between the first and second frontal lobes. Many of the convolutions were pale and of the consistency of cartilage. The larger swellings were depressed in the centre, and over them the pia mater was adherent. Numerous small, hard nodules were found in the ependyma of the ventricles. The cerebellum, basal ganglia and spinal cord were normal; the kidneys contained a number of small, hard, circumscribed nodes, consisting chiefly of involuntary muscle fibres. Microscopically, no degenerated fibres were found in the sclerotic areas. The pyramidal cells were either slightly swollen or atrophic. They were much altered in shape, and their position was irregular. The tangential fibres had disappeared, and at the periphery of the cortex nothing was left excepting a coarse neuroglia tissue. The other regions in the brain were normal. The blood vessels exhibited marked hyalin degeneration, and were in part obliterated. In the sclerotic areas they were more numerous than normal. The author calls attention to the presence of other signs of degeneration, but is rather inclined to believe that the disease is the result of hereditary syphilis, and, on account of the normal position of the chief sulci, he is inclined to believe that it developed late fœtal life. He admits, however, that it probably is only an exaggeration of the condition usually found in epileptic brains.

Scarpatetti refers to an additional case, that, on account of its misleading title, escaped my attention, and has not been included in the literature. The changes were apparently slight. (Koch: "Ein Fall von Idiotie in Folge von Application der Zunge." Neurologisches Centralblatt, 1887.)

No.	Name.	Age at death.	Sex.	Neuropathic heredity.	Syphilis.	Tumors of the kidneys.	Trauma.	Congenital defects.
1	Bourneville	15	f.	0		1		
2	Bourneville & Brissaud	4	m.	1				1
3	Bourneville & Bonnaire	5	m.	1		1	1	
4	Bourneville & Bonnaire	5	m.	1	?	1		
5	Bourneville & Bonnaire	5¾	m.	1		1		
6	Hartdegen	2 days	m.	0		0		1
7	Pollak	3	f.	?				
8	Bruckner	22	f.	0				
9	Pocci	68	m.					
10	Simon	2½	f.	1				
11	Schule							
12	Bucholz							
13	Thibal		m.					
14	Bucholz		m.					
15	Bucholz		m.					
16	Bucholz		f.					
17	Wilmarth							
18	Wilmarth							
19	Wilmarth							
20	Wilmarth							
21	Wilmarth							
22	Wilmarth							
23	Henoch	2			?	1		1
24	Berdez	4	m.	0	?			
25	Bourneville	11	m.	1	1			
26	Tedeschi	28	f.					
27	Spiller		m.			0		
28	Jurgens	6 mos.	m.	0	0	1	?	1
29	Sailer	15	m.	1		1		
30	Scarpatetti	20	f.	1	?	1		1

1=yes. 0=no.

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